comprising a melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist, wherein said compound is administered to the periphery of said animal in an amount effective to measurably decrease body weight or reduce the rate of weight gain in said animal as compared to in the absence of administration of said compound, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal.

4. (Once Amended) The method of Claim 1, wherein said compound is selected from the group consisting of melanocyte stimulating hormone (MSH), a biologically active fragment of MSH, a homologue of MSH having MSH agonist activity, a peptide mimetic of MSH having MSH agonist activity, a non-peptide mimetic of MSH having MSH agonist activity, and a fusion protein comprising an MSH protein or a biologically active fragment thereof.

5. (Reiterated) The method of Claim 1, wherein said compound is selected from the group consisting of α-MSH, β-MSH and γ-MSH.

6. (Once Amended) The method of Claim 1, wherein said compound is a peptide mimetic of MSH having MSH agonist activity.

7. (Reiterated) The method of Claim 1, wherein said compound is an analog of a peptide having an amino acid sequence represented herein by SEQ ID NO:2.

8. (Once Amended) The method of Claim 1, wherein said compound is an α-MSH analog selected from the group consisting of:

a. [Ac-Cys^4, D-Phe^7, Cys^{10}] α-MSH, wherein said Cys residues are connected by a disulfide bond;

b. Ac-[Nle^4, X_{aa}^5, His^6, X_{aa}^7, Arg^7, Trp^9, X_{aa}^{10}]-NH_2, (SEQ ID NO:3)

wherein X_{aa}^5 is Glu or Asp, X_{aa}^7 is Phe or D-Phe and X_{aa}^{10} is a dibasic amino acid; Lys; ornithine; 2,4, diaminobutyric acid; or 2,3 diaminopropionic acid (Dpr);

c. Ac-[Cys^4, Cys^{10}]α-MSH_{1-13}-NH_2;

d. R_1-W-X-Y-Z-R_2,

wherein R_1 is selected from the group consisting of Ac-Gly-, Ac-Met-Glu-, Ac-Nle-Glu- and Ac-Tyr-Glu-;

W is selected from the group consisting of -His- and -D-His-;

X is selected from the group consisting of -Phe-, -D-Phe-, -Tyr, -D-Tyr-, (-pNO_2)D-Phe^7-;

Y is selected from the group consisting of -Arg- and -D-Arg-;

Z is selected from the group consisting of -Trp- and -D-Trp-; and,

R_2 is selected from the group consisting of $-NH_2$, -Gly-NH_2, and -Gly-Lys-NH_2;

e. Ac-Ser-Tyr-Ser-M-Glu-His-D-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH_2 (SEQ ID NO:4),

wherein M is selected from the group consisting of Met, Nle, and Cys;

f. [Nle^4, D-Phe^7]-α-MSH;

g. [Nle^4, D-Phe^7]-α-MSH_{4-10};

h. [Nle^4, D-Phe^7]-α-MSH_{4-11};

i. [Nle^4, D-Phe^7,D-Trp^9]-α-MSH_{4-11};

j. [Nle^4, D-Phe^7]-α-MSH_{4-9}; and

k. Ac-[Nle^4, AA^5, D-Phe^7, AA^{10}]-R_1 or Ac-[Nle^4, AA^5, D-Phe^7, AA^{11}]-R_2;

wherein AA^5 may be either a L- or D- amino acid having an omega amino or carboxyl group in the side chain, e.g., α,γ-diaminopropionic acid, α,γ-diaminobutyric acid, Orn, Lys, α,β-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

a4 Cont.

wherein AA^{10} may be diaminopropionic acid, α,γ-diaminobutyric acid, Orn, Lys, α,β-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein R_1 is the designation α-$MSH_{1-13}NH_2$, α-$MSH_{1-12}NH_2$, α-$MSH_{1-11}NH_2$, α-$MSH_{4-13}NH_2$, or α-$MSH_{4-10}NH_2$;

wherein AA^{11} may be L- or D- amino acid having an omega-amino or carboxyl group in the side chain, e.g., α,β-diaminopropionic acid; α,γ-diaminobutyric acid, Orn, Lys, α-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein R_2 is the designation α-$MSH_{1-13}NH_2$, α-$MSH_{1-12}NH_2$, α-$MSH_{1-11}NH_2$, α-$MSH_{4-13}NH_2$, or α-$MSH_{4-10}NH_2$; and,

wherein Xxx may be from 1 to 5 a-amino acid residues each of which may be of L- or D- configuration, or a linear or branched chain spacer.

9. (Once Amended) The method of Claim 1, wherein said compound is a peptide comprising an amino acid sequence represented by SEQ ID NO:1.

a4 Cont Sub C3

10. (Once Amended) The method of Claim 1, wherein said MSH compound has the following identifying characteristics: (1) an ability to bind to a melanocortin receptor that is expressed in peripheral tissues; and, (2) a biological activity selected from the group consisting of stimulation of lipolysis and inhibition of the uptake of fatty acids by adipocytes.

a5

13. (Once Amended) The method of Claim 1, wherein said compound binds to a melanocortin receptor expressed in the peripheral tissues with a higher affinity than to melanocortin-4 receptors (MC4-R).

16. (Reiterated) The method of Claim 1, wherein said compound does not bind to MC4-R under physiological conditions.

18. (Reiterated) The method of Claim 1, wherein said compound does not activate MC4-R under physiological conditions.

19. (Reiterated) The method of Claim 1, wherein said therapeutic composition is administered transdermally.

20. (Reiterated) The method of Claim 1, wherein said therapeutic composition is administered topically.

21. (Reiterated) The method of Claim 1, wherein said therapeutic composition is administered parenterally.

23. (Reiterated) The method of Claim 1, wherein said therapeutic composition is administered in a controlled release formulation.

24. (Reiterated) The method of Claim 1, whereby administration of said compound is insufficient to cause a statistically significant change in the appetite of said animal as compared to before administration of said compound.

a6

25. (Once Amended) The method of Claim 1, wherein said compound is administered in a dose of from about 0.1 μg to about 10 mg per kg body weight of said animal.

26. (Once Amended) The method of Claim 1, wherein said compound is administered in a dose of from about 1 μg to about 10 mg per kg body weight of said animal.

27. (Once Amended) The method of Claim 1, wherein said compound is administered in a dose of from about 40 μg to about 1 mg per kg body weight of said animal.

a7

28. (Once Amended) The method of Claim 1, wherein said compound is from about 0.1% to about 90% of said therapeutic composition by weight.

29. (Once Amended) The method of Claim 1, wherein said compound is from about 0.1% to about 1% of said therapeutic composition by weight.

31. (Once Amended) The method of Claim 1, wherein said decrease in body weight in said animal can be measured within at least about one week of said step of administering said compound.

32. (Once Amended) The method of Claim 1, wherein said animal has serum leptin levels between about 0 ng/ml and 50 ng/ml prior to said step of administration.

33. (Once Amended) The method of Claim 1, wherein said animal has serum MSH levels between about 0 ng/ml and 10 ng/ml prior to said step of administration.

34. (Once Amended) The method of Claim 1, wherein said animal has a ratio of serum MSH levels to serum leptin levels of greater than about 1:100 prior to said step of administration.

35. (Once Amended) The method of Claim 1, wherein said animal is a human having a body mass index (BMI) of greater than 27 kilograms per square meter prior to administration of said compound.

a8

36. (Once Amended) The method of Claim 1, wherein said composition further comprises another body weight regulating agent.

37. (Once Amended) The method of Claim 36, wherein said another body weight regulating agent is leptin.

38. (Once Amended) The method of Claim 37, wherein said composition comprises a ratio of said MSH compound to leptin of about 1:100.

39. (Once Amended) The method of Claim 37, wherein said composition comprises said leptin in a dose of from about 0.1 μg to about 100 mg per kg body weight of said animal.

53. (Reiterated) The method of Claim 1, wherein said animal is a human.

54. (Reiterated) The method of Claim 1, wherein said composition further comprises an antagonist of MC4-R.

55. (Once Amended) The method of Claim 1, wherein said composition further comprises an agent that inhibits binding of said MSH compound to an MC4-R.

56. (Once Amended) The method of Claim 1, wherein said composition further comprises an agent which inhibits said MSH compound from entering the central nervous system of said animal.

59. (Once Amended) A method of decreasing the body weight or reducing the rate of weight gain in an animal, comprising administering to an animal a melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist in an amount effective to bind to melanocortin receptors expressed by said animal in said animal's peripheral tissues, said effective amount:

(a) being insufficient to substantially change the appetite of said animal after said step of administering as compared to before said step of administering;

(b) being between about 0.1 μg and about 10 mg per kg of body weight of said animal;

(c) being sufficient to affect a biological activity selected from the group consisting of:

(i) lipolysis; and,

(ii) uptake of fatty acids by adipocytes in said animal; and,

(d) being effective to measurably decrease the body weight or reduce the rate of weight gain of said animal after said compound has been administered to said animal.

66. (Once Amended) A method for regulating metabolic efficiency in an animal, comprising:

(a) measuring serum melanocyte stimulating hormone (MSH) levels in an animal;

(b) identifying animals having serum MSH levels of less than about 0.1 ng/ml; and,

(c) administering to the periphery of said animals identified in (b) a composition comprising a compound selected from the group consisting of a melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist, and leptin, wherein said MSH compound is administered in an amount effective to increase serum MSH levels in said animal to a level effective to produce a result selected from the group consisting of stimulating lipolysis and inhibiting fatty acid uptake in said animal.

a11 cont

67. (Reiterated) The method of Claim 66, wherein said compound is administered in an amount effective to produce a measurable decrease in body weight of said animal.

68. (Once Amended) A therapeutic composition that regulates the peripheral melanocortinergic and/or leptinergic pathways of energy homeostasis in an animal, comprising:

a12

a. a melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist; and,

b. a body weight regulating agent that is not a MSH compound.

70. (Once Amended) The therapeutic composition of Claim 68, wherein said MSH compound is selected from the group consisting of melanocyte stimulating hormone (MSH), a biologically active fragment of MSH, a homologue of MSH having MSH agonist activity, a peptide mimetic of MSH having MSH agonist activity, a non-peptide mimetic of MSH having MSH agonist activity, and a fusion protein comprising an MSH protein or a biologically active fragment thereof.

a13

73. (Once Amended) The therapeutic composition of Claim 68, wherein said MSH compound is an analog of a peptide having an amino acid sequence represented herein by SEQ ID NO:2.

a14

74. (Once Amended) The therapeutic composition of Claim 68, wherein said MSH compound is an α-MSH analog selected from the group consisting of:

a. [Ac-Cys^4, D-Phe^7, Cys^{10}] α-MSH, wherein said Cys residues are connected by a disulphide bond;

b. Ac-[Nle^4, $X_{aa}{}^5$, His^6, $X_{aa}{}^7$, Arg^7, Trp^9, $X_{aa}{}^{10}$]-NH_2, (SEQ ID NO:3)

wherein X_{aa}^5 is Glu or Asp, X_{aa}^7 is Phe or D-Phe and X_{aa}^{10} is a dibasic amino acid; Lys; ornithine; 2,4,-diaminobutyric acid; or 2,3 diaminopropionic acid (Dpr);

c. Ac-[Cys^4, Cys^{10}]α-$MSH_{1-13}NH_2$;

d. R_1-W-X-Y-Z-R_2,

wherein R_1 is selected from the group consisting of Ac-Gly-, Ac-Met-Glu-, Ac-Nle-Glu- and Ac-Tyr-Glu-;

W is selected from the group consisting of -His- and -D-His-;

X is selected from the group consisting of -Phe-, -D-Phe-, -Tyr, -D-Tyr-, (-pNO_2)D-Phe^7-;

Y is selected from the group consisting of -Arg- and -D-Arg-;

Z is selected from the group consisting of -Trp- and -D-Trp-; and,

R_2 is selected from the group consisting of -NH_2, -Gly-NH_2, and -Gly-Lys-NH_2;

e. Ac-Ser-Tyr-Ser-M-Glu-His-D-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH_2 (SEQ ID NO:4),

wherein M is selected from the group consisting of Met, Nle, and Cys;

f. [Nle^4, D-Phe^7]-α-MSH;

g. [Nle^4, D-Phe^7]-α-MSH_{4-10};

h. [Nle^4, D-Phe^7]-α-MSH_{4-11};

i. [Nle^4, D-Phe^7,D-Trp^9]-α-MSH_{4-11};

j. [Nle^4, D-Phe^7]-α-MSH_{4-9}; and

k. Ac-[Nle^4, AA^5, D-Phe^7, AA^{10}]-R_1 or Ac-[Nle^4, AA^5, D-Phe^7, AA^{11}]-R_2;

wherein AA^5 may be either a L- or D- amino acid having an omega amino or carboxyl group in the side chain, e.g., α,γ-diaminopropionic acid, α,γ-diaminobutyric acid, Orn, Lys, α,β-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein AA^{10} may be diaminopropionic acid, α,γ-diaminobutyric acid, Orn, Lys, α,β-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein R_1 is the designation α-$MSH_{1-13}NH_2$, α-$MSH_{1-12}NH_2$, α-$MSH_{1-11}NH_2$, α-$MSH_{4-13}NH_2$, or α-$MSH_{4-10}NH_2$;

a14 Cont.

wherein AA^{11} may be L- or D- amino acid having an omega-amino or carboxyl group in the side chain, e.g., α,β-diaminopropionic acid; α,γ-diaminobutyric acid, Orn, Lys, α-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein R_2 is the designation α-$MSH_{1-13}NH_2$, α-$MSH_{1-12}NH_2$, α-$MSH_{1-11}NH_2$, α-$MSH_{4-13}NH_2$, or α-$MSH_{4-10}NH_2$; and,

wherein Xxx may be from 1 to 5 a-amino acid residues each of which may be of L- or D- configuration, or a linear or branched chain spacer.

75. (Once Amended) The therapeutic composition of Claim 68, wherein said MSH compound is a peptide comprising an amino acid sequence represented by SEQ ID NO:1.

80. (Once Amended) The therapeutic composition of Claim 68, wherein said composition comprises said MSH compound in a dose of from about 0.1 μg to about 10 mg MSH compound per kg body weight of an animal to which said composition is to be administered.

81. (Once Amended) The therapeutic composition of Claim 68, wherein said composition comprises said MSH compound in a dose of from about 1 μg to about 10 mg MSH compound per kg body weight of an animal to which said composition is to be administered.

82. (Once Amended) The therapeutic composition of Claim 68, wherein said composition comprises said MSH compound in a dose of from about 40 μg to about 1 mg MSH compound per kg body weight of an animal to which said composition is to be administered.

85. (Once Amended) The therapeutic composition of Claim 68, wherein said body weight regulating agent is leptin.

86. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises a ratio of said MSH compound to leptin of 1:100.

87. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises a ratio of said MSH compound to leptin of 1:25.

88. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises a ratio of said MSH compound to leptin of 1:10.

89. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises said leptin in a dose of from about 0.1 μg to about 100 mg leptin per kg body weight of an animal to which said composition is to be administered.

90. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises said leptin in a dose of from about 0.1 μg to about 10 mg leptin per kg body weight of an animal to which said composition is to be administered.

a16 cont

91. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises said leptin in a dose of from about 1 μg to about 10 mg leptin per kg body weight of an animal to which said composition is to be administered.

93. (Reiterated) The therapeutic composition of Claim 68, further comprising a pharmaceutically acceptable excipient.

94. (Reiterated) The therapeutic composition of Claim 93, wherein said pharmaceutically acceptable excipient prolongs the presence of said therapeutic composition in the bloodstream of a animal.

a17

95. (Once Amended) A method for treating an affective and mood disorder in an animal, comprising administering to an animal at risk for or suffering from an affective mood disorder a therapeutic composition comprising a melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist, wherein said MSH compound is administered to the periphery of said animal in an amount effective to measurably ameliorate said disorder in said animal as compared to in the absence of administration of said compound, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal.

a18

98. (Once Amended) The method of Claim 1, wherein said animal is at risk for or suffering from an obesity-associated disorder.

99. (Reiterated) The method of Claim 98, wherein said obesity-associated disorder is selected from the group consisting of non-insulin dependent diabetes mellitus, cardiovascular disease, cancer, hypertension, osteoarthritis, stroke, respiratory problems, and gall bladder disease.

a19

100. (Once Amended) A method for treating a reproductive disorder in an animal, comprising administering to an animal at risk for or suffering from a reproductive disorder

a therapeutic composition comprising a melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist, wherein said MSH compound is administered to the periphery of said animal in an amount effective to prevent or ameliorate said disorder as compared to in the absence of administration of said compound, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal.

a 19 cont

102. (Once Amended) The method of Claim 1, wherein said animal is at risk of or suffering from undesired body weight which is a side effect resulting from administration of a pharmaceutical compound.

a 20

103. (Reiterated) The method of Claim 102, wherein said pharmaceutical compound is selected from the group consisting of valproic acid, lithium, tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRI).

Please add the following new Claims 108-114.

108. (Added) A method to increase the body weight or reduce the rate of weight loss in an animal, comprising administering to said animal a therapeutic composition comprising a melanocyte stimulating hormone (MSH) antagonist compound, wherein said compound is administered to the periphery of said animal in an amount effective to measurably increase body weight or reduce the rate of weight loss in said animal as compared to in the absence of administration of said compound, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal.

a 21

109. (Added) The method of Claim 108, wherein said compound has the following identifying characteristics: (1) an ability to bind to a melanocortin receptor that is expressed in peripheral tissues of said animal; and, (2) a biological activity selected from the group consisting of inhibition of lipolysis and stimulation of the uptake of fatty acids by adipocytes.

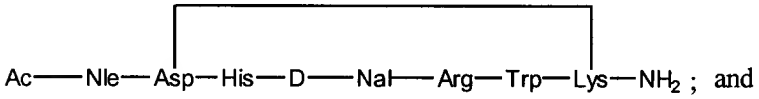
110. (Added) The method of Claim 108, wherein said MSH antagonist compound is selected from the group consisting of a fragment of MSH having MSH antagonist activity, a homologue of MSH having MSH antagonist activity, a peptide mimetic of MSH having

MSH antagonist activity, a non-peptide mimetic of MSH having MSH antagonist activity, and a fusion protein comprising a peptide having MSH antagonist activity.

111. (Added) The method of Claim 108, wherein said antagonist compound is a peptide mimetic of MSH having MSH antagonist activity.

112. (Added) The method of Claim 108, wherein said antagonist compound is an MSH analog selected from the group consisting of:

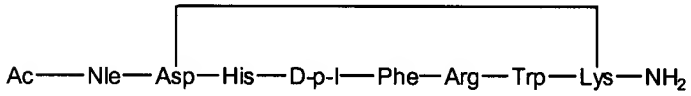
a.



; and (SEQ ID NO:5)

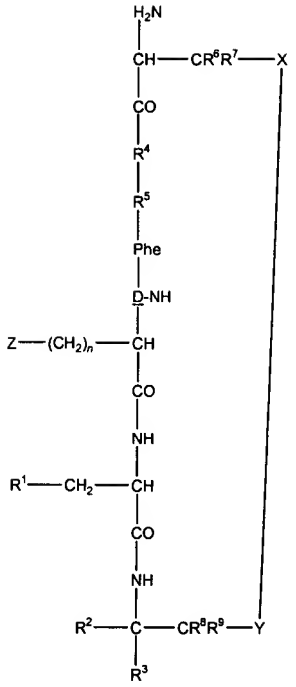
a21 cont.

b.



(SEQ ID NO:6); and,

c.



wherein R^1 is a substituted or unsubstituted aromatic radical;

R^2 is hydrogen or a methyl group;

R^3 is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

R^4 is glutamic acid, alanine, -amino butyric acid, valine, leucine or isoleucine;

R^5 is histidine, glutamic acid, alanine, valine, leucine or isoleucine;

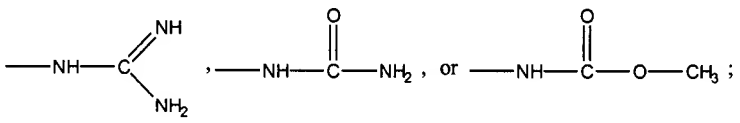
a21 cont.

R^6 and R^7, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

R^8 and R^9, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

X and Y are sulfur, methylene, SO or SO_2;

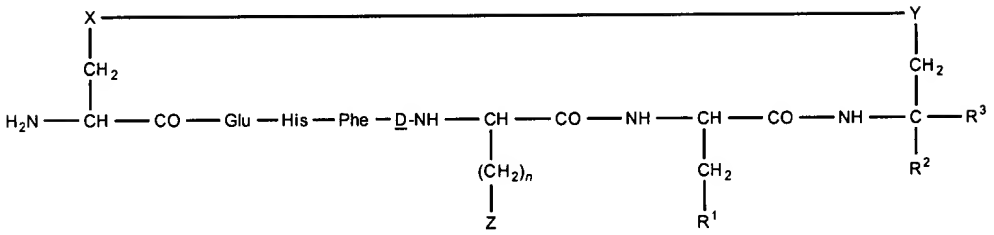
Z is $-NH_2$,



and,

n is an integer greater than or equal to 2; and,

d.



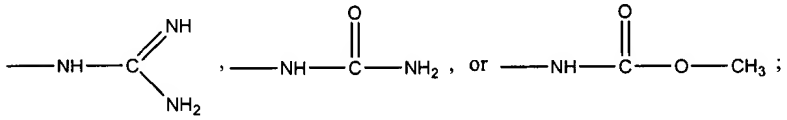
wherein R^1 is phenyl, indole, p-hydroxyphenyl, p-aminophenyl, imidazole, 1-naphthyl adamantyl or alkylphenyl, 2-naphthyl;

R^2 is hydrogen or a methyl group;

R^3 is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

X and Y are sulfur, methylene, SO or SO_2;

Z is $-NH_2$,



and,

n is an integer greater than or equal to 2; and wherein the cyclized portion of the compound is conformationally restricted in a manner which is compatible with the reactivity of the compound with receptors of the central nervous system.

113. The method of Claim 108, wherein said animal suffers from an eating disorder selected from the group consisting of anorexia and bulemia.

114. The method of Claim 108, wherein said animal suffers from a wasting syndrome selected from the group consisting of: wasting disease, cachexia and sarcopenia.